Pseudohyperkalemia in a Non-compliant CLL Patient: A Case Study

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ABSTRACT

Elevated serum and/or plasma potassium is an occasional occurrence in patients presenting with severe leukocytosis. The term pseudohyperkalemia applies to these conditions in which accurate testing on an acceptable specimen rules out actual hyperkalemia. It is important to correctly diagnose pseudohyperkalemia quickly in order to avoid treatment error. A non-compliant patient previously diagnosed with chronic lymphocytic leukemia is presented for discussion of appropriate laboratory testing and diagnosis in pseudohyperkalemia.

ABBREVIATIONS: CLL - Chronic lymphocytic leukemia, SLL - Small lymphocytic lymphoma, BMP - Basic metabolic panel, WBC - White blood cell

INDEX TERMS: Pseudohyperkalemia, hyperkalemia, chronic lymphocytic leukemia, leukocytosis, potassium

Clin Lab Sci 2017;30(2):84-86

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INTRODUCTION

A previously non-compliant 50-year old male diagnosed with chronic lymphocytic leukemia (CLL) was admitted to a 635-bed tertiary care community hospital to receive chemotherapy. Admission laboratory testing included a basic metabolic panel (BMP), calcium, and uric acid obtained from a sodium heparin blood collection tube. Results of this initial test and a subsequent recollection indicated an extremely elevated plasma potassium. Investigation of preanalytic variables including order of draw, patient medication, and general health status of the patient failed to resolve the questionable hyperkalemia results. Subsequent collection and testing using a serum sample centrifuged at a reduced speed revealed a normal serum potassium level. A discussion of this patient's diagnostic testing will explain why the erroneous potassium value was initially obtained and offer suggestions to avoid similar errors.

CASE PRESENTATION

Patient history

The patient was admitted to the hospital as a non-compliant CLL patient for the purpose of chemotherapy. According to the 2008 World Health Organization Classification of Lymphoid Neoplasms, CLL is categorized as a mature B cell lymphoma with a designation of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).[1] A primary involvement of the lymph nodes and other lymphoid tissues is consistent with a diagnosis of SLL; alternatively, if the primary site of involvement is the bone marrow and the peripheral blood, then a diagnosis of CLL is rendered.[1] While CLL and SLL represent two different clinical manifestations, they are thought to originate from a common unknown clonal line of B cells.[1] CLL is the most commonly diagnosed leukemia in the Western world with median diagnosis at 70 years of age and a higher prevalence among males than females.[2,3] Diagnosis of CLL is often an incidental finding from blood work performed for some other medical reason. An elevated white blood cell (WBC) count and/or absolute clonal lymphocytosis (≥ 5,000 cells/μL) is commonly found upon initial presentation.[2] Peripheral smear findings include many small, mature B lymphocytes with

clumped chromatin and minimal cytoplasm.[2,3] A defining feature of CLL is the presence of smudge cells seen on the peripheral blood smear.[2] Smudge cells are nuclear remnants created by the shearing force on the fragile, malignant B cells during blood smear preparation. Disease progression in CLL patients is quite variable with some patients experiencing a rapid clinical course and other patients having few symptoms for a decade or more.[4]

Laboratory Testing

Upon admission to the hospital, the attending physician ordered a basic metabolic panel, calcium and uric acid. Following centrifugation of the heparinized collection tube, the laboratory technologist noted slight hemolysis and possible lipemia. The patient's initial laboratory results are shown in Table 1. The patient's potassium was extremely elevated at greater than 14.0 mmol/L. Suspecting hemolysis as the cause of a potentially falsely elevated potassium, the laboratory technologist requests recollection of the specimen.

Laboratory results for the recollected heparinized plasma specimen are also shown in Table 1. The recollected sample appeared lipemic, but unhemolyzed. Since the potassium result was again greater than 14 mmol/L despite the lack of apparent hemolysis, the technologist investigated other sources of preanalytic error. Upon speaking with the patient's nurse, the technologist confirmed that the patient was alert and well, and was not taking any medication other than the prescribed chemotherapy. Furthermore, the phlebotomist and hematology department confirmed that no EDTA tubes were collected on this patient during the current day, eliminating the possibility of cross-over contamination of the heparinized specimen. However, the hematologist noted that the patient was diagnosed with CLL and had a white blood cell (WBC) count of 808,000/microliter.

Suspecting the high WBC count as the source of elevated potassium, the technologist requested a second sample recollection, with an order for a serum sample rather than heparinized plasma. After allowing the sample to clot, the technologist centrifuged the specimen using a soft spin (low rpm) technique which resulted in a serum sample that appeared unhemolyzed and clear. Patient results from the serum sample are shown in Table 1. Significantly, the patient's serum potassium was normal at 4.7 mmol/L.

DISCUSSION

Pseudohyperkalemia, or artificially elevated potassium observed *in vitro* without a corresponding elevation of potassium or evidence thereof *in vivo*, is frequently observed secondary to hemolysis. Because of the high intracellular concentration of potassium, pseudohyperkalemia can also be observed secondary to thrombocytosis or leukocytosis.[5] Of these three conditions, leukocytosis as a cause for pseudohyperkalemia, is the least recognized. In the case under discussion, the observed pseudohyperkalemia is attributed to leukocytosis.

Although poorly understood, it is believed that several factors contribute to the leukocytic pseudohyperkalemia. These include the use of vacuum blood collection tubes[6]

Table 1. Laboratory results

Laboratory Test	Initial Plasma Sample Result	Recollected Plasma Result	Recollected Serum Result	Reference Interval Plasma (P) / Serum (S)
Sodium	120 mmol/L	123 mmol/L	142 mmol/L	137-145 mmol/L (P/S)
Potassium	>14.0 mmol/L	>14.0 mmol/L	4.7 mmol/L	3.5-4.5 mmol/L (P) 3.5-5.3 mmol/L (S)
Chloride	106 mmol/L	106 mmol/L	107 mmol/L	98-107 mmol/L (P/S)
Carbon Dioxide	22 mmol/L	21 mmol/L	23 mmol/L	23-30 mmol/L (P/S)
Glucose	92 mg/dL	93 mg/dL	121 mg/dL	75-110 mg/dL (P/S)
BUN	17 mg/dL	17 mg/dL	17 mg/dL	9-20 mg/dL (P/S)
Creatinine	1.01 mg/dL	1.02 mg/dL	1.11 mg/dL	0.66-1.25 mg/dL (P/S)
Calcium	8.2 mg/dL	6.7 mg/dL	9.4 mg/dL	8.4-10.2 mg/dL (P/S)
Uric Acid (uricase)	1.3 mg/dL	1.3 mg/dL	0.6 mg/dL	3.5-8.3 mg/dL (P/S) male

and/or pneumatic tube specimen transportation systems,[7] prolonged storage, tourniquet use, and recentrifugation.[8,9] Additionally, and significant to this case, increased WBC fragility observed in leukemias is also implicated in leukemic pseudohyperkalemia.[10]

Clearly, identification of pseudohyperkalemia as distinct from true hyperkalemia is critical to effective patient treatment. In the case described, the distinction was possible through collection of a serum specimen processed with soft centrifugation which minimized the effect of increased cell fragility on WBC lysis. The false "lipemia" observed in the first two plasma samples was, in fact, due to the presence of lysed WBC in the two plasma samples. There is disagreement in the literature as to whether a serum or plasma sample is preferable to minimize pseudohyperkalemia in patients with leukocytosis, thrombocytosis, or erythrocytosis.[5] Some data suggest that clot formation protects fragile cells, preventing hemolysis. Other data suggest that clot formation increases the occurrence of pseudohyperkalemia.[5] Therefore, perhaps the most reliable method to distinguish pseudohyperkalemia from true hyperkalemia is by measurement of potassium from a whole blood specimen using a blood gas analyzer.[11] The minimization of preanalytic variables including tourniquet use, clotting, transportation, centrifugation, and storage inherent in blood gas testing will likely lead to the most accurate potassium results in patients with increased cellularity.

CONCLUSION

This case study demonstrates the importance of several factors in achieving accurate results: specimen collection and processing, knowledge of the patient's underlying medical condition, and an understanding of the causes of falsely elevated potassium. Integration of the chemistry technologist's own observations, patient history obtained from other medical professionals, and an ability to recognize the signs of falsely elevated potassium ultimately resulted in the reporting of an accurate potassium level for this patient. Increased awareness among clinical laboratory professionals of leukocytosis, a lesser known cause of pseudohyperkalemia, in addition to understanding methods to obtain an accurate potassium result, are key to optimal patient care.

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